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AMERICAN FOREST & PAPER ASSOCIATION

DATE: August 12, 2002

TO: Dr. Scott A. Masten
Office of Chemical Nomination & Selection
NIEHS/NTP
P.O. Box 12233, MD A3-07
Research Triangle Park, NC 27709

RE: **Request for Public Comment on Substances Nominated for Toxicological Studies (67 FR, June 12, 2002 pgs: 40329-40333)**

Dear Dr. Masten:

The American Forest & Paper Association (AF&PA) wishes to provide the following comments in response to the nomination and recommendation of turpentine [CAS:8006-64-2] for toxicological studies.

AF&PA is the national trade association of the forest products industry. AF&PA members produce pulp, paper and paperboard from both virgin and reclaimed fiber, as well as lumber and wood products. Crude sulfate turpentine (CST) is produced by many of AF&PA's members as a buy-product of the pulping process. CST is a major source of turpentine and other distillation by-products produced and sold in commerce. Therefore, AF&PA has a direct interest in the proposed testing.

Basis for Nomination

The support document gives as a basis for nomination widespread human exposure and reports of kidney toxicity in chronically exposed humans. In addition it is stated that studies would offer potential "mechanistic insight into the human relevance of chemically induced _2_-globulin and resulting kidney toxicity and carcinogenic responses in exposed animals".

Section 9.1.1.4 of the support document notes several references which discuss studies of potential kidney toxicity in humans. None of the studies or reports cited, however, provide any clear evidence that exposure to turpentine is associated with chronic kidney toxicity in humans.

It is properly noted that early studies of painters gave conflicting results. Moreover, as discussed in the paper by Chapman (1941) referenced in this section, exposure to lead in lead-based paints is a suspect factor. Given the lack of clear evidence for chronic human kidney effects of turpentine, the mechanistic rational for the proposed study also seems to be without scientific merit.

Gentoxicity

The support document indicates that no genotoxicity studies were found for turpentine. The document however omits any references to genetic testing of turpentine constituents. Such data are relevant, and should be included. We are aware of several published studies that have investigated potential genetic effects of turpentine constituents. These are listed and briefly summarized below. The full citations are attached.

1. Rockwell et.al. (1979)

   Camphene and alpha-pinene, assayed on TA98 or TA100 in the presence of S9, did not exhibit mutagenicity.

   Ether extracts of 24-hour urine samples of rats fed camphene were weakly mutagenic toward TA100, but not TA98. No mutanenic activity was detected when the direct urine samples were assayed with TA100 and TA98 either in the presence or absence of beta-glucuronidase. A negative response was also observed when the aqueous fractions of the ether extractions were assayed with both tester strains.

2. Florin et. al. (1980)

   In a screening assay using the Ames test, neither limonene, alpha-pinene nor beta-pinene were found to be mutagenic.

3. Connor et. al. (1985)

   Limonene and alpha-pinene were not found to be mutagenic using a battery of bacterial test strains.

4. Sasaki et. al. (1989)

   Neither camphene, limonene nor beta-pinene showed evidence of sister chromatid exchange in Chinese hamster ovary cells.

5. Turner et. al. (2001)

   Limonene administered in the diet was not mutagenic in the liver or kidney of male Big Blue rats.

AF&PA appreciates the opportunity to comment on the nomination and proposed toxicological studies. If you have any questions concerning the comments, please contact me at 202-463-2587.

Sincerely,

John L. Festa, Ph. D
Senior Scientist

Attachment

References

Chapman E.M., Observations on the effect of paint on the kidneys with particular reference to the role of turpentine. J. Industrial Hygiene and Toxicology, 23 277-289 (1941).

Connor T. H., Theiss, J.C., Hanns HA; Monteith DK. and Matney TS. Genotoxicity of organic chemicals frequently found in the air of mobile homes. Toxicology Letters, 25 33-40 (1985).

Florin I., Rutberg L., Curvall M. and Enzell C. Screening of tobacco smoke constituents for mutagenicity using the Ames test. Toxicology, 18 219-232 (1980).

Rockwell P., and Raw I. A mutagenic screening of various herbs, spices, and food additives. Nature and Cancer, 1 (4) 10-15 (1979).

Sasaki YF., Imanishi H., Ohta T., and Shirasu Y. Modifying effects of components of plant essence on the induction of sister-chromatid exchange in cultured Chinese hamster ovary cells. Mutation Research, 226 103-110 (1989).

Turner SD., Tinwell H., Piegorsh W., Schmezer P. and Ashby J. Mutagenesis 16 (4) 329-32 (2001).